PATENT
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A METHOD AND APPARATUS FOR DISPENSING SEPARATOR GEL IN A BLOOD COLLECTION TUBE

1. Field of the Invention

The present disclosure relates generally to a method and apparatus for separating blood components in a blood collection device. Specifically, the present disclosure relates to a method for the separation of a light serum portion of blood from a heavy cellular portion of blood, the blood collection device used to collect and separate blood, and manufacturing the blood collection device. More particularly, the present disclosure relates to a method of dispensing separator gel in a blood collection tube for improving gel barrier stability and adhesion of the gel to a tube wall during the separation process.

2. Prior Art

Blood collection devices for separating the lighter serum portion of a blood sample from the heavier cellular portion thereof are well known. These devices usually comprise a collection tube containing a thixotropic gel and a contact activated clotting agent. The gel has a specific gravity intermediate the specific gravity of the serum and the cellular phases of the blood sample.

After a sample of blood has been deposited into the collection tube, the contact-activated clotting agents begin to clot the blood sample by activating clotting factors within the blood. The agent facilitates the clotting process until the blood is completely coagulated. The agent coagulates substantially all of the blood sample in order for the subsequent serum separation process to be complete. Once the blood has coagulated, the collection tube is placed in a centrifuge to separate the lighter serum from the heavier coagulum portion. Coagulum is defined as the cellular portion and fibrin clot of the blood as opposed to the lighter serum portion of the blood. During centrifugation, the gel on the bottom of the collection tube is displaced upwardly through the blood sample until it reaches its equilibrium position at the interface between the

serum and the coagulum. In this position, the gel forms a barrier between the serum and the coagulum which permits the lighter serum to be either decanted directly from the collection tube, or sampled using automated blood analyzing equipment, without interference from the coagulum.

It has long been known in the art that human blood can be readily centrifuged to effect a separation of the blood into its lighter serum and heavier coagulum portions. The specific gravity of the serum portion of human blood is between approximately 1.026 and 1.031, while the specific gravity of the coagulum portion of human blood is between approximately 1.092 and 1.095. The specific gravity of the gel is therefore chosen to be approximately between 1.032 and 1.091, so that once a blood sample is centrifuged, the gel will form an effective barrier between the serum and the coagulum. A preferred gel to be used with the method of the present disclosure is a thixotropic composition described in U.S. Patent No. 4,140,631 to Okuda et al., entitled "Sealant for Separation of Serum or Plasma, and It's Use," the entire disclosure of which is hereby incorporated herein by reference. As described in Okuda et al., the preferred thixotropic gel is a polymer essentially consisting of at least one compound from the group of alkyl acrylates and alkyl methacrylates, which has a specific gravity of 1.03 to 1.08 and a viscosity of about 5,000 to 1,000,000 cps at a shear rate of 1 second when measured at 25°C. However, any suitable gel-like composition which can be used as a barrier between blood portions separated in a centrifuge is felt to fall within the spirit and scope of the present disclosure.

This type of gel is adapted to migrate or flow from the bottom of the tube under the influence of centrifugation to the interface position between the serum and the coagulum portions of the blood and adhere to the inside surface of the collection tube wall to form a barrier between the blood portions to maintain a separation therebetween. However, this migration causes an attendant loss of gel along the tube wall, thereby requiring initial placements of larger amounts of gel in the tube in order to insure the formation of a strong enough mechanical barrier to properly separate the two portions of blood during centrifugation.

Weak adhesion of the gel to the collection tube's inner surface during centrifugation of the blood sample is a problem with prior art blood collection devices. Such weak adhesion of the gel is due to the blood sample wetting the inner surface of the blood collection device prior to the migration of the gel. This wetted inner surface inhibits the natural adhesive properties of the gel, thereby preventing the gel from forming a strong adhesive bond thereto. U.S. Patent No. 4,257,886 seeks to overcome this deficiency by disclosing a blood separation assembly that coats the bottom portion of the collection tube with a hydrophobic material that resists wetting of the collection tube's inner surface and allows the gel to form a strong adhesive bond to the inner surface during centrifugation.

Another method of addressing the gel migration problem with its attendant loss of adhesion is found in U.S. Patent No. 4,417,981 which attempts to overcome the problems associated with gel migration by dispensing the gel in a separator assembly located in the central portion of the collection tube near the eventual formation of the gel barrier. The pre-placement and dispensation of the gel in a separator assembly permits the gel to quickly adhere to the tube wall during centrifugation without migration and attendant loss of gel. However, the above method of dispensing gel using a device incurs further expense in manufacturing an additional element to attain proper separation of the blood sample.

Referring to FIGS. 1-4, the prior art method of dispensing separator gel 3 and separating a blood sample into two portions is shown. The method involves utilizing a commonly known gel dispensing apparatus (not shown) to dispense a predetermined amount of gel 3 into the bottom 5 of a collection tube 2. Contact-activated clotting powder or particles 6 are then deposited inside collection tube 2 for eventual activation of clotting factors within blood 7 after blood 7 is added to collection tube 2.

As shown in FIG. 2, a predetermined amount 4 of blood 7 is added to collection tube 2 and contact clot-activating material 6 within collection tube 2 begins to coagulate blood 7 before collection tube 2 is placed in a centrifuge (not shown) for centrifugation of blood 7. Contact clot-activating material 6 promotes clot formation and includes but is not limited to glass and silica. Referring now to FIG. 3, during centrifugation of blood 7 in collection tube 2, gel 3

becomes less viscous and begins to migrate upward along an inner surface 8 of collection tube 2 until it reaches an interface point 9 where lighter serum portion 10 of blood 7 begins to separate from heavier coagulum portion 11. Interface point 9 is a result of the two portions of blood, serum 10 and coagulum 11, being physically separated due to the effect of their different specific gravities during centrifugation. As shown in FIG. 4, separation gel 3, having a specific gravity intermediate that of serum 10 and coagulum 11, has migrated to interface point 9 between the two blood portions. At interface point 9, gel 3 forms a mechanical barrier 12 inside collection tube 2 that physically separates the two blood portions and prevents serum 10 from being contaminated by coagulum 11.

As of yet, nothing in the prior art has addressed the problem of developing an efficient means of dispensing gel that does not suffer from either attendant loss of gel caused by migration or weak adhesive properties when gel barrier 12 is formed.

Therefore, there exists a need in the blood collection art for an improved means of dispensing gel into a collection tube in an inexpensive and efficient manner which promotes both quick formation of the barrier separating the two blood portions and a strong adhesion of the barrier to the collection tube's inner surface once the gel barrier is formed.

Summary of the Invention

In brief summary, the present disclosure relates to a means of dispensing gel for separation of the lighter serum portion and the heavier coagulum portion of a blood sample in a blood collection tube. The preferred method of dispensing the gel comprises utilizing a gel dispensing apparatus with a nozzle head or like portion having a plurality of openings. The gel dispensing apparatus dispenses either a continuous band of gel around the central portion of the collection tube or a plurality of discrete stripes that flow to form a continuous band pattern around the central portion of the collection tube. Once the gel is so dispensed around the central portion of the collection tube, the tube is ready for accepting a blood sample for eventual separation in a centrifuge where the dispensed gel will form a barrier between the serum portion

and the coagulum portion of the blood sample while exhibiting strong adhesive properties, i.e., few to no points of fluid communication between blood portions.

The present disclosure includes a method of dispensing gel into a tube having opposed open and closed ends, a central body portion between the opposed open and closed ends, and an interior surface formed by the central body portion and the closed end, comprising the steps of: providing the tube, providing a gel dispensing apparatus for dispensing a gel into the tube, placing a portion of the apparatus inside the tube, dispensing the gel from the portion of the apparatus onto an interior wall surface formed by the central body portion, and terminating the dispensation of the gel.

The present disclosure further includes a blood collection device for use in separating blood into different portions comprising a tube having a central body portion, opposed closed and open ends, and an interior surface with gel dispensed on an interior wall surface thereof. Optionally, contact clot-activating particles may be placed within the device.

The present disclosure still further includes a method of separating blood into different portions using the aforementioned blood collection device optionally containing contact clot-activating particles comprising the steps of: placing a blood sample inside the blood collection device, centrifuging the device containing the blood collection sample wherein centrifuging the device and the blood sample permits the gel to flow inwardly from the interior wall surface to form a barrier between the different portions of the blood sample after centrifugation is complete.

Accordingly, a principal object of the present disclosure is to provide an efficient and inexpensive method for dispensing gel in a collection tube for use in separating a blood sample into portions.

Another important object of the present disclosure is to provide an improved method of dispensing gel that requires minimal or no migration of the gel along the tube wall to form a barrier between portions of blood being separated during centrifugation.

A further object of the present disclosure is to provide a method of dispensing gel that forms a continuous and stable barrier in a short period of time and exhibits strong adhesive properties, i.e., few to no points of fluid communication between the blood portions.

Another important object of the present disclosure is to provide a means of dispensing gel in discrete stripes or a continuous band around the interior wall surface of a collection tube.

A further object of the present disclosure is to provide a blood collection device that has gel dispensed on the interior wall portion of a tube.

Another principal object of the present disclosure is to provide a method of using a tube with gel dispensed on the inner surface thereof for separation of blood into separate portions.

Additional objects, advantages and novel features of the present disclosure will become apparent to those skilled in the art upon examination of the following more detailed description and drawings in which like elements of the present disclosure are similarly numbered throughout.

Brief Description of the Drawings

FIG. 1 shows the prior art method of dispensing gel at the bottom of a blood collection tube;

FIG. 2 shows the prior art blood collection tube of FIG. 1 after a blood sample has been added thereto;

FIG. 3 shows the prior art migration of gel toward the serum/coagulum interface during centrifugation of the blood sample;

FIG. 4 shows the prior art blood collection tube after centrifugation of the blood sample and the formation of the gel barrier at the interface between the two portions of the blood;

FIG. 5 shows the present method of dispensing gel on the interior wall portion of a collection tube using a nozzle head for dispensing gel in a continuous band around the interior wall portion of the collection tube;

FIG. 6 shows a top section view of the blood collection tube of FIG. 5 showing the gel on the inner surface of the tube with an opening therethrough;

FIG. 7 shows the blood collection tube of the present disclosure demonstrating the method of determining the lower and upper limits for dispensing gel; and

FIG. 8 is a perspective view of the gel dispensing apparatus showing the alternative embodiment of a continuous opening at the nozzle head.

Detailed Description

In one embodiment, in accordance with the present disclosure, a method of dispensing gel within a blood collection tube is shown in FIG. 5. A blood collection apparatus 20, including a conventional collection tube 21 having an opposed open end 23 and closed end 34 is made of a material which is non-interactive with a blood sample 35, such as but not limited to plastic, glass, plastic-lined glass or glass-lined plastic. Collection tube 21 has a separator gel 22 which is a thixotropic substance dispensing into the central portion of tube 21 between opposed open end 23 and closed end 34 prior to adding a blood sample 35.

Gel 22 is placed within tube 21 by using a positive displacement metering apparatus 24 that uses a nozzle head 25 for dispensing a gel or the like. Nozzle head 25 includes one or more openings but preferably a plurality of openings 26 located at its free distal end 31. In an alternative embodiment, one opening 126 is provided at free distal end 31 of nozzle head 25. Opening 126 is a continuous opening around the periphery of an exterior surface 128 of nozzle

head 25, as illustrated in FIG. 8. It is contemplated that opening 126 may be disposed about the entire circumference about only a portion thereof or intermittently disposed about nozzle head 25. Although one or more openings 26 can be utilized for the present disclosure, a plurality of openings 26 will be exemplified throughout the remainder of this description for purposes of simplicity only.

Plurality of openings 26 dispense gel 22 onto inner surface 29 of tube 21 in discrete stripes 30 that flow to form a circumferential band pattern around collection tube 21. Preferably, gel 22 is dispensed in discrete stripes 30, although any suitable configuration that ultimately flows to form one or more continuous circumferential bands around inner surface 29 of collection tube 21 is included, within the spirit and scope of the present disclosure.

Prior to dispensing gel 22, nozzle head 25 is placed inside collection tube 21 such that openings 26 are positioned at a predetermined first limit, such as, for example, a predetermined lower point 27 to begin dispensing gel 22 along inner wall surface 29 of collection tube 21. As gel 22 is dispensed through openings 26, collection tube 21 is slowly drawn downward so as to move closed end 34 away from nozzle head 25 until openings 26 reach a predetermined second limit, such as, for example, a predetermined upper limit 28 near open end 23. As the dispensing procedure is about to terminate, nozzle head 25 is slightly ahead of gel 22 flow, thereby forming a discontinuous circumferential pattern 32 at predetermined upper limit 28. It is contemplated that during dispensation from plurality of openings 26, a discontinuous circumferential pattern 32 is formed at the end of dispensation in a crown shape design, but any suitable pattern may be made. Once the dispensation of gel 22 is terminated, gel 22 flows and adheres to inner surface 29 forming a circumferential band around the central portion of collection tube 21 between the predetermined upper and lower limits, 28 and 27, respectively. As shown in FIG. 6, gel 22, after flow thereof has ceased, forms the cirumferential band with discontinuous pattern 32 at the top of the circumferential band and an opening 33 through which blood sample 35 may initially pass before centrifugation and formation of the gel barrier. After gel 22 has set or flow has ceased, collection apparatus 20 is ready for blood sample 35 to be added for centrifugation and separation, as described above.

The location of the upper and lower limits, 28 and 27, respectively, in dispensing gel 22 forming the concentric band on inner surface 29 of collection tube 21 depends on the size of collection tube 21 being utilized and the volume of blood sample 35 to be added to collection tube 21. Upper and lower limits, 28 and 27, respectively, are measured from a location on collection tube 21 adjacent open end 23. Referring to FIG. 7, a general formula for determining the upper and lower limits, 28 and 27, respectively, for gel 22 dispensation will be discussed. X is a variable that represents a linear dimension, such as, for example, the length of collection tube 21 which holds a predetermined volume of blood sample 35 added to collection tube 21 prior to centrifugation. In determining the lower and upper limits for gel placement, 27 and 28, respectively, variable X is multiplied by predetermined constants, C_{LL} for the lower limit 27 and C_{UL} for upper limit 28.

These constants are established by one skilled in the art based on factors including the configuration and dimension of collection tube 21, the type of centrifuge (angled, horizontal, etc.), the particular gel configuration, the quantity of gel, the volume of blood, etc. Based on, for example, these factors, it has been established that C_{UL} is approximately 0.30 and that C_{LL} is approximately 0.70. It is envisioned that the constants C_{UL} and C_{LL}, may vary within the numerical range of 0.30-0.70 to respectively facilitate determination of upper limit 27 and lower limit 28.

The general formulas used to determine upper limit 28 and lower limit 27 are shown below:

$$\text{Lower limit } 27 = X \cdot C_{LL}$$

$$\text{Upper limit } 28 = X \cdot C_{UL}$$

For example, if C_{LL} and C_{UL} are established as being 0.70 and 0.31, respectively, as described above, for a particular tube to achieve a particular desired configuration, lower limit 27 and upper limit 28, may be easily determined by knowing the length of collection tube 21 which holds the predetermined volume of the drawn blood sample 35 added to the collection tube 21 having a length of 100 mm. To illustrate, if the predetermined volume of blood sample 35 is added to collection tube 21, lower limit 27 for dispensing gel 22 would be 70 mm and upper limit 28 would be 31 mm as set forth below.

Lower limit 27 = 100 mm x .7 = 70 mm

Upper limit 28 = 100 mm x .31 = 31 mm

Thus, gel 22 would be dispensed between a range of 31 mm to 70 mm from the location on collection tube 21 adjacent open end 23 to form the circumferential band. It is contemplated that collection tube 21 may have variously dimensioned diameters, such as, for example, 13 mm, 16 mm, etc., according to the requirements of a particular application. It should be noted that the formula would be varied accordingly if more than one circumferential band would be desired for further separation techniques known in the art.

The above example is used for the purpose of illustrating upper and lower limits, 28 and 27, respectively, for dispensing gel 22 in collection tube 21 in accordance with the present disclosure. The above formula in accordance with the principals of the present disclosure advantageously provides that a firm mechanical gel barrier is formed after centrifugation regardless of the type of centrifuge used to separate blood sample 35.

The method of dispensing gel 22 of the present disclosure, as described, has the advantage of limited migration of gel 22 during centrifugation while promoting a stronger mechanical barrier after centrifugation. Moreover, dispensing gel 22 on the interior wall portion between upper and lower limits, 28 and 27, respectively, of collection tube 21 has the further advantage of requiring less gel 22 than required in prior art methods in which gel 22 migration was utilized. For example, prior art methods for dispensing gel 22 dispense approximately 2.2 grams of gel 22 to form a sufficient barrier after centrifugation of blood sample 35 while the present disclosure requires approximately 1.4 grams of gel 22 to form the same strong barrier. Thus, the present disclosure requires approximately 36% less gel 22 which creates a significant cost savings.

The method of separating blood sample 35 into different portions using blood collection apparatus 20, similar to the present disclosure will be now illustrated. The method of separating a blood sample 35 using blood collection apparatus 20 having contact clot-activating particles 6

previously deposited inside apparatus 20 comprises the step of providing a blood sample 35 inside apparatus 20. After blood sample 35 is deposited, blood sample 35 is then centrifuged, wherein centrifuging blood sample 35 permits gel 22 to flow inwardly as blood sample 35 travels through opening 33 until a barrier is formed between the different phases of blood sample 35 once centrifugation is complete.

Blood collection apparatus 20 of the present disclosure may likewise optionally contain contact clot-activating particles such as but not limited to carbon, silica, fumed silica, glass and the like. Likewise, the entire interior surface or a portion of the interior surface of blood collection tube 21 of the present disclosure may optionally be sprayed with a water and/or silica mixture to prevent blood from sticking to the sides of collection tube 21. This spray is preferably applied before dispensing of gel 22, as described above.

Optionally, the interior of blood collection apparatus 20 of the present disclosure may be sprayed with an ethylene copolymer such as but not limited to polyethylene oxide and/or polydimethyl siloxane to promote gel 22 binding to the wall.

Although particular embodiments of the disclosure have been shown, it is not intended that the disclosure be limited thereby, instead the scope of the present disclosure is intended to be limited by the appended claims.